Study ABO/Rh system with Endothelial Inflammatory Factors in Iraqi Arab Female with Diabetes Mellitus Type II

Asmaa M. Salih* Isam N. Salman**
Rajaa M. Kaduhm ***

Received 18, June, 2013 Accepted 18, August, 2013

Abstract:

Diabetes mellitus type II is a disorder of metabolism and complex diseases affected by genetic environmental factors and associated with inflammation. The symptoms of type II diabetes develop gradually, which are associated with increased blood concentration of marker of the endothelial inflammatory factors. The expression of adhesion molecules, including E-selectin, intracellular adhesion molecule-1(ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) on the surface of vascular endothelial cells to help leukocyte stick to other surrounding tissues. Many researchers have made attempts to determine the significance of particular ABO phenotype for the susceptibility to diseases. Many reports show a strong association with the ABO blood groups and diabetes Type II. Dysfunction increases risk of type II diabetes among women with low level of subclinical incident diabetes. For that reason the present study has been designed to study the association between diabetic, endothelial dysfunction and blood group in Iraqi Arab diabetic women. Sixty patients of Iraqi Arabs female with previous diagnosed diabetic type II involved in this study and comparison with twenty controls matched in age, sex and ethnic groups. Both of patients and control divided into four sub groups according to the blood types. We evaluated endothelial inflammatory factors ICAM, VCAM and E-Selectin. Present data showed a significant difference in the serum level of ICAM-1 and E-section between diabetes mellitus type II patients and controls while there were no significant differences in the serum level of VCAM-1. In conclusion, significant increasing of the level of ICAM-1 and E-selectin made them as a risk factors to predict diabetes progression, women who carry blood group A, B and AB show appositive association with diabetic, while females who carry blood group O less susceptible to infected with diabetes mellitus type II.

Key words: endothelial inflammatory factors, ICAM, VCAM and E-selectin . Diabetic millets typ2 and blood groups.

Introduction:

Diabetes mellitus type II (DM TII) is a disorder of metabolism and complex diseases affected by genetic environmental factors and associated with inflammation [1] it is the response of sensitivity individuals to the glucose. Lowering action of insulin could vary greatly. This variability in insulin sensitivity lead to the

recognition of the existence of insulin resistance (part of the cause of type 2 diabetes) [2] .Several studies shown a relationship between systemic inflammation and diabetes.

Meanwhile, inflammation represents a protective response to control infection and promote tissue repair [3]. Certain pro-inflammatory stimuli can

^{*}Biology department/ college of science for women, Baghdad University.

^{**}National Diabetes Centre/ Al-Mustansiryia University,

^{***}Msc. Student, / Baghdad University /College of Science for Women/Biology Department

elicit the expression of adhesion molecules, including E-selectin, adhesion intracellular molecule-1(ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) on the surface vascular endothelial of Circulating levels of all three endothelial inflammatory markers were positively and significantly associated with diabetes risk [4]. The endothelial leukocytes associated and membrane protein has been known for it is importance in stabilizing cell-cell interaction and facilitating leukocyte endothelial Trans membrane during inflammatory condition [5]. Since there discovery the ABO blood groups have been of a great interest, many researchers have made attempts to determine the significance of particular ABO phenotype for the susceptibility to diseases ,because blood groups are known to have phenotypic frequency differences and these blood systems have been used as markers of ancestry studying so the distribution of these markers may help in understanding the disproportional incidence of type II diabetes [3] .Rh is the most complex of blood group systems, embracing 45 distinct antigens, the absence or presence of which combine to exhibit an individual's, Rh blood group type Rh positive present in over 85% of the random population .The Rh antigen are encoded by two highly homologous and closely linked genes on the Short arm of chromosome 1 [6]. They have been found that ABO glycotransferase have broader impact atherosclerotic than simply throw modulation of thrombosis has linked the ABO locus to circulating levels of intracellular soluble adhesion molecule-1 (sICAM-1) and soluble Eselectin [7]. Furthermore endothelial dysfunction increases risk of type 2 diabetes among women with low level of subclinical incident diabetes [8], so that elevated circulating levels of

soluble adhesion molecule used as markers of endothelial dysfunction. Morever their association with type 2 diabetes have been reported [7]. For that reason the present study have been designed to study the association between diabetic, endothelial dysfunction and blood group in Arab Iraqi diabetic women.

Materials and Methods:

Sixty patients of Iraqi Arabs diagnosed with previous female diabetic type II were examined by the physicians of national of diabetes centre in Al-Mustansirya University. We chosen women who suffer from diabetic type II less than six years and age between twenty to the end of fifty nine years, no history of any metabolic no medical history disorder. hypertension, no thyroid dysfunction, no regular alcohol or smoking and no pregnancy, with twenty individuals matched in age, sex and ethnic group. The study main groups (patients and controls) divided into four sub groups according to the class of blood groups (group A, B, AB and

Various parameters are studies to be compared between patient and control groups:

- 1-ABO / Rh Blood group Kit (agglutination), (Atlas medical).
- 2-sICAM-1 Kit (eBioscience, high performance immunoassays, Platinum Elisa ready-to-use sandwich). By ELISA
- 3-sVCAM-1 kit (eBioscience, high performance immunoassays, Platinum Elisa ready-to-use sandwich). By ELISA
- 4-sE-selectin kit (eBioscience, high performance immunoassays, Platinum Elisa ready-to-use sandwich). By ELISA

The data analyses were done by using SAS (2010) system to effect of difference faction in study parameters. Least signification difference-LSD test and chi square were used to compare between means in this study

Results:

The results show the comparison between patient and control groups according to the level of inflammatory endothelial parameters. The ICAM-1 (ng/ml) parameter show significant increasing level in patients group (54.08 ± 2.21) compared to control (47.19 ± 3.26) . Also the E-selectin (ng/ml) show significant increasing between deference patient group (16.25 ± 0.85) compared to control group (11.36 ± 1.11) while the VCAMsignificant 1(ng/ml)show non decreasing between patient (34.81 ± 9.88) and control (35.32 \pm 6.87) in table 1.

Table 1 .statistical analysis between main study group according to the serum level of inflammatory endothelial parameters (ng/ml).

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Parameters	Main stue Mean	T-test				
	Control Patients					
	group	group				
ICAM	47.19 ±	54.08 ±	8.50 *S			
(ng/ml)	3.26	2.21	0.30 '3			
VCAM	35.32 ±	34.81 ±	35.10			
(ng/ml)	6.87	9.88	NS			
E- selectin	11.36 ±	16.25 ±	3.20*S			
(ng/ml)	1.11	0.85	3.20"3			

S = significant differences (P<0.05)* NS= Non significant

The comparison among main study groups and subgroups according to the concentration of ICAM-1 (ng/ml) patient subgroups A show none significant differences compared to patients sub group B (table 2) .In contrast there were significant differences among A (57.24 \pm 3.66) and B (57.83 \pm 3.47) patient subgroups

compared to AB (47.66 ± 7.22) while there were subgroups, significant difference between AB and (52.40 ± 3.94) subgroups concentration of ICAM-1. Consequently, mean while, there were no significant differences between each type of patient subgroups and control subgroups among A, B and O patients subgroups except significant differences were found between patients sub groups type B compared to control sub group 0.05). Furthermore control subgroups AB showed non significantly increased for ICAM-1 level compared to patient sub groups AB .At the same time there were no significant differences among all control sub groups.

Table 2 .The comparison among study main group and subgroups according to the serum Level of ICAM-1 (ng/ml).

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main	Study sub groups					
study groups	A	В	AB	О		
Patients(Mean ± SE)	57.24 ± 3.66 b	57.83 ± 3.47 b	47.66 ± 7.22 a	52. 40 ± 3.9 4 ab		
Control (Mean ± SE)	45.05 ± 9.64 a	49.00 ± 3.10 a	56.30 ± 2.80 a	46. 08 ± 4.5 2 a		
T-test	P≥0.05 NS	P≤0.05 S*	P≥0.05 NS	P≥0 .05 NS		

S= significant ($P \le 0.05$) * NS= non significant ($P \ge 0.05$)

The different letters for row mean significant differences p≤0.05 *.

From this figure (1) we noticed the level of ICAM-1 which is decreased in the sera of patients sub groups type AB compared to control sub groups type AB, in contrast to the others comparison among other

groups, other patients sub groups blood types show increased level of ICAM compared to the control sub groups of the same type.

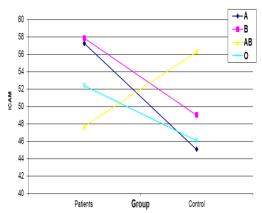


Fig.1. Effect of blood group in ICAM (compare between patients and control

The distribution of study groups according to the blood groups and their relation with the concentration of VCAM. Table (3) show that there were significant difference among patients subgroup in concentration of VCAM compared with each others, actually patients sub groups AB (84.33 \pm 67.7) showed highly significant differences compared with others patients subgroup, followed by patients subgroup B (35.46 \pm 13.1) which was significantly differ from the others while there were non significant differences between O (26.94± 7.77) patient subgroup and A (19.93 ±2.66) patients subgroup consequently. There significant differences were also between patients sub groups (A, AB, O) compared to the control subgroups of the same type, and no significant between subgroups difference $(P \ge 0.05)$ for patients and control. At the same time the comparison among all control subgroups for blood type with each others were non significant $(P \ge 0.05)$.

Table 3. The comparison among study main groups and subgroups according to the serum level of VCAM-1 (ng/ml)

Main study	Study subgroups					
groups	A B		AB	О		
Patients (Mean ± SE)	19.93 ± 2.66 a	35.46 ± 13.1 b	84.33 ± 67.7 c	26.94 ± 7.77 a		
Control (Mean ± SE)	29.25 ± 3.85 a	37.65 ± 5.35 a	28.45 ± 1.35 a	38.11 ± 11.46 a		
T-test	P≤0.05 S	P≥0.05 NS	P≤0.05 S	P≤0.05 S		

S= significant NS= non significant

The different letters for row mean significant differences ($P \le 0.05$)*.

At figure 2 patient subgroup AB has the highly significant mean of VCAM among all study subgroups, while the control subgroup A has the lowest serum mean level of VCAM-1. At the same time healthy individuals who carry allele A (control sub group A and AB) illustrated the lowest concentration of VCAM-1, so three sub groups(patients A ,control A and control AB were showed decreased level of VCAM-1, inversely sub groups with allele B were showed increased level of VCAM-1.

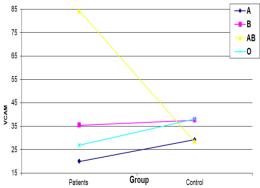


Fig. 2. Effect of blood group in VCAM (compare between patients and control)

The comparison among study main groups and subgroups according

to the concentration of E-selectin (ng/ml). Table (4) show non significant differences among patient subgroups in concentration of E-selectin at the same patient subgroups AB significantly differ from patient subgroups B and patients subgroups O. while non significant differ recorded among patients sub groups for blood types A ,B and O . The comparison among control sub groups show highly significant differences between control sub group O with others control sub groups except control sub groups AB, there were non significant differences between AB control sub group and B control sub groups. Control sub groups O recorded the highest mean level E-selectin among control sub groups ,without significant difference with control sub group AB, Moreover control sub groups AB were significantly higher than control subgroup A , while the differences between control sub group B and control subgroup Α were significant. There were significant difference between patients sub group and control subgroups for each type of blood group except the difference between patients sub group type O (14.72 ± 1.24) and control sub group type O (13.59 ± 0.98) were non significant $(P \ge 0.05)$

Table 4. The comparison among study main groups and subgroups according to the serum level of Eselectin (ng/ml).

Main study	Study subgroups					
groups	A	В	AB	О		
Patients (Mean± SE)	17.40 ± 1.87 ab	15.15 ± 1.71 a	20.86 ± 2.27 b	14.72 ± 1.24 a		
Control (Mean ± SE)	6.25 ± 2.73 a	9.40 ± 0.20 ab	9.57 ± 6.53 bc	13.59 ± 0.98 c		
T-test	P≤0.05 S	P≤0.05 S	P≤0.05 S	P≥0.05 NS		

S= significant NS= non significant

The different letters for row mean significant differences $(P \le 0.05)^*$.

Figure 3 shows increased level in all subgroups of patient compared to the same subgroups except the O subgroups. The mean of serum level for two O subgroups (patient and control) were closed without any significant difference. On the other hand the concentration of E-selectin for B controls subgroups and B control sub group were slightly differ without any significant difference.

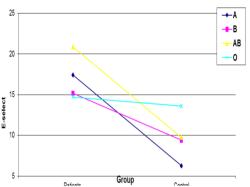


Fig.3. Effect of blood group in E-select (compare between patients and control)

Table 5 show there were many females with type O in both group patients and controls (41 .7-60%) followed by blood type A for both group patient and control (23.3-20%) then followed by blood type B for both groups (20-10%) and least distributed was blood type AB (15-10%). Chisquare shows significant difference among all study subgroups, moreover there were significant differences within subgroups type A, B and O. While any other comparison were non significant. From the same table we noticed females who carrying allele A (from blood group A and AB) show the high ratio (23.3%, 15%) when added with each other (38,3%), inversely allele B show less collected ratio(20%+15=35%) even when we do that the ratio still more than the collected ratio for control. Blood group A,B and AB show positive association with diabetes mellitus type II (P < 0.05) which implied that A,B and AB blood group patients have high chance of DM TII because blood group A, B and AB were more common in patients than control .The value was 23.3 %, 20 % and 15 % for patients with blood group A ,B and AB respectively ,and for control 20 % ,10 % and 10 % inversely for blood group O patients 41.7 % were less numerous than control 60 % ,that mean blood group O show significant negative association with DM TII by chi -square ($p \le 0.05$)

Table 5: distribution of phenotype frequency of ABO blood groups in

studied groups.

	0 -					
	Phenotype frequency					
Blood	Pat	ients	ents Controls		Total sample	
groups	No.	%	No.	%	No.	%
A	14	23.3	4	20	18	22.5
В	12	20	2	10	14	17.5
AB	9	15	2	10	11	13.7 5
О	25	41. 7	12	60	37	46.2 5
Total	60	100	20	10 0	8	10 0

 X^2 =7.719 DF=3 (S) p≤0.05 (total comparison for sub study groups).

 X^2 =14.807 DF=2 (S) p≤0.05 (B, AB and O comparison within groups).

Other comparisons were non significant ($P \ge 0.05$).

Table 6 shows the distribution of Rh blood groups. The Rh positive showed the most frequent of blood type between patients and control (93.3-90%) while the Rh negative blood group show the less distribution between patients and control (6.7-6%) with significant differences ($x2=p \le 0.05$) That means Rh positive was more common in patients and Rh negative less common.

Table 6: Distribution of Rh blood group in studied groups

Rh	Patients		Control		Total	
group	No.	%	No.	%	No.	%
Rh+	56	93.3	18	90	74	92.5
Rh-	4	6. 7	2	10	6	7.5
Total	60	100	20	100	80	100

 X^2 =0.578 d f=1 (NS) P \geq 0.05 (total comparison).

Discussion:

From all present data, we found that circulating levels of endothelial soluble adhesion molecules (E-selectin. ICAM-1 and VCAM-1) in sera of control groups women were unstable. With significant increased of ICAM-1 (ng/ml) and E-selectin (ng/ml) level between patients and control sub groups, these results agree with previous study demonstrated that each ICAM-1 and E-selectin increased in significantly diabetes mellitus patients [4].that may referred that those women will subsequently developed clinical diabetes [9] because E-selectin ICAM-1 were strongly significantly related to an increased risk of diabetes across diverse ethnic .Moreover [10, 11] circulating levels of endothelial soluble adhesion molecules including selectin and ICAM-1 at baseline were significantly elevated among initially healthy women who subsequently developed clinical diabetes.

The comparison among study main groups and subgroups according to the serum level of ICAM-1 (ng/ml) which show significant differences among A and B patient subgroups compared to AB patients subgroups, these data disagree with a previous study which demonstrated there was less enhanced response of plasma ICAM-1[12], while there were no significant differences between AB and O subgroups in concentration of

ICAM-1. This differences among study subgroups refers to fluctuation in the level of ICAM-1 that may associate with the Clinical progress of disease, investigation especially The demonstrate that soluble levels in blood samples from type II diabetes have been observed patients significantly high ICAM-1 levels compared to none diabetic control subjects [11, 13].

The present comparison illustrated that the patients showed increase level of VCAM-1 compared to control for all blood sub groups types ,these result agree with previous data show increased level of VCAM-1 inflammatory condition in during which related with it increased cellular expression on adhesion molecules on endothelial cells and other tissue type[14]. From table 3 and figure 2, we can concluded that female who carrying allele A may tend to decrease the expression of VCAM-1 factor because females who carrying allele A showed decreased level of VCAM-1 except the patients sub group AB and that increased level in may return to allele B especially patients sub group AB showed the highly level of VCAM-1

In our study even in patient subgroup AB (20.86 ±2.27) showed the highly significant mean comparison among study main groups and subgroups according to serum level of E-selectin (ng/ml) but the mean of the controls subgroup AB (9.57±6.53) was not the highest one among control subgroups with the highest standard error than any other ones that means the levels of E-selectin was fluctuate in healthy individuals and maybe there is an association between E-selectin and blood group. Actually E-selectin tends to show an elevated level even in healthy females and these phenomena needs further investigate in future. These results

were agree with [8], which show higher significant with patient than control for the risk of type II diabetes by baseline levels of E-selectin, while other research show the related between E-selectin and type II diabetes that identified association between a cluster of markers at the ABO locus on chromosome 9q34 and plasma sE-selectin concentration [15].

The present data positive significant association among A, B and AB blood type with DM Type II while it was a negative association with blood, while it was a negative with blood group O (patient 41.7 % versus control 60%) which means that females with blood type A. B and AB are more susceptible for DM TII while females with blood group O are less susceptible for DM. The result disagree with previous report, which mentioned that blood type A,B and O are at a higher risk of being diabetic Most data on association [16] . between the distribution of the ABO types diseases blood and conflicting some previous studies reporting no association [17, 18], in positive contrast others showed association [19], because most of the populations where evidence association between genetic markers and type II DM has been found are hybrid populations form by recent mixing of parental populations [20]. Females with blood type A (23.3%) ,B(20%) and AB(41.7%) are at a higher risk of being diabetic but that an argue result because according to the level of inflammatory endothelial factors, the blood group AB show the higher level of VCAM-1 among other blood group. Meanwhile females in the present data who carrying allele B less likely to were have diabetic patients [21].Female who carry allele A are more susceptible to progress DMTII more than female who are carrying allele B, this result disagree with a previous study have been reported that allele A was less appear in DMTII [21].

In our data regarding Rh blood group a high frequency of the Rh positive was observed between patient and control .with significant which differences mean it commonest, the dominance of positive Rh phenotype was noted in Iraqi population in previous study [22, 23, 24] also in different Iraqi ethnic groups like Kurd [25] and Sabian [23]. On the other hand Rh blood system may play some rules in the process of glucose metabolic and may influence the clinical expression of DM type II [17]. In our study, the blood group O in total sample and Rh positive were the most dominant among Iraqi population, representing 46. 25% and (92.5%) this result agree with report by [26]. Present finding about elevated serum levels of E-selectin and ICAM showed that increased level we can provided a factors that we can used them as a predictive factors which reflects the progression of disease, moreover, female with A,B, AB and Rh positive were more susceptible to develop DM TII which means there is association between DM TII and blood groups, but we still need large and more advance studies on other females ethnic groups and males to confirm these results, and to understand the genetic association at molecular level.

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دراسة نظام ABO/Rh مع العوامل الألتهابية لبطانة الأوعية الدموية في مرضى السكري من النوع الثانى لدى النساء العراقيات العربيات

عصام نوری سلمان ** رجاء مسلم کاظم ***

أسماء محمد صالح *

*جامعة بغداد/كلية العلوم للبنات/ قسم علوم الحياة

** الجامعة المستنصرية/ المركز الوطني للسكر

*** جامعة بغداد/كلية العلوم للبنات/ قسم علوم الحياة

الخلاصة

يعد مرض السكري من الامراض المعقدة التي يرافقها اضطراب ايضي ويحدث بسبب تداخل العوامل الوراثية والبيئية المرتبطةبالالتهاب وتتطور اعراض المرض تدريجيا ويرتبط بزيادة العوامل الالتهابية لبطانة الاوعية وهي (جزئ الالتصاق بين الخلايا ,1-ICAM جزئ الالتصاق بالاوعية الدموية 1 الدموية الدموية الدموية البيضاء على الاتصاق بالبطانة وقد والتي يتم عرضها على سطح خلايا بطانة الاوعية الدموية لتساعد الخلايا البيضاء على الاتصاق بالبطانة وقد حاول العديد من الباحثين ايجاد علاقة معنوية بين الطراز المظهري لمجاميع الدم OB والاستعداد للمرض وتوجد بحوث تؤكد وجود علاقة قوية بين المرض ومجاميع الدم والاضطراب الوظيفي لهذه العوامل يؤدي الى الالتهابية ومجاميع الدم والاصابة بالسكري لدى النساء العراقيات العربيات، وشملت الدراسة 06 مريضة بالسكري من النوع الثاني مع 20 امراة كمجموعة ضابطة مطابقة للمرضى بالعمر والجنس والعرق، ثم قسمت بالسكري من النوع الثاني مع 10 امراة كمجموعة ضابطة مطابقة للمرضى بالعمر والجنس والعرق، ثم قسمت والسيطرة، اذ سجل ارتفاع كل من 1-CAM والسائل الدم VCAM والعوامل التنبوءية التي تستخدم لتشخيص تطور المرض وبنفس الوقت اظهرت النساء الحاملات لفصائل الدم A,B,AB ارتباطا موجبا بالسكري بينما النساء الحاملات لفصائل الدم A,B,AB ارتباطا موجبا بالسكري بينما النساء الحاملات لفصيلة الدم O استعدادا اللسكري من النوع الثاني.

البحث مستل من رسالة الباحث الثالث